DRAFT
PROTOCOL FOR CROSS-VALIDATION EXPERIMENTS

1. **Objective**: Determine if the analyses conducted at Covance Harrogate and MDSPS Lincoln for nicotine, cotinine, trans-3'-hydroxycotinine, nicotine-N-glucuronide, cotinine-N-glucuronide, and , trans-3'-hydroxycotinine-O-glucuronide in human urine provide equivalent results.

2. **Procedure**: Each laboratory will be provided 24 coded urine samples. Each laboratory will analyze each sample in triplicate, according to their previously validated analytical method. Individual results for each analysis will be provided in an Excel spreadsheet to Philip Morris for evaluation by January 31, 2003.

3. **Acceptance Criteria**: Data will be evaluated by a regression analysis and a bias analysis. The two analytical methods for nicotine and its metabolites will be considered equivalent if the 95% confidence interval of the mean relative difference is within ± 20% for all the samples with concentrations > LLOQ. At the LLOQ of the less sensitive analytical method, the two analytical methods will be considered equivalent if the 95% confidence interval of the mean relative difference is within ± 25% for all the samples with concentrations = the LLOQ of the less sensitive analysis.

4. **Results**: Data tabulated by sample number and results from the Philip Morris statistical analyses will be available to both laboratories at the completion of our evaluation.

Signatures:

Mark Bentley, Covance Harrogate Date

Vincent Andaloro, MDS Pharma Services Date